Ramamurthy S, Hoffman J, Guanethidine Study Group. Intravenous Regional Guanethidine in the Treatment of Reflex Sympathetic Dystrophy/Causalgia: A Randomized, Double-Blind Study. Anesth Analg 1995;81:718-23.

Design: Randomized Controlled Trial

Population/sample size/setting:

- 57 patients (mean age 40, 24 men, 33 women) with RSD symptomatic less than 3 months treated at 16 study sites affiliated with the University of Texas
- Inclusion criteria were age over 12 with no more than 3 months of CRPS I or II (defined as allodynia, hyperalgesia, and/or hyperesthesia in the extremity consistent with CRPS)
- Excluded if recent MI/CVA, suspected pheochromocytoma, psychiatric problem, ulcer, angina, etc
- Excluded for current anticoagulant, TCA, MAOI, or other autonomic drugs

Main outcome measures:

- Pain Rating Index (PRI) of McGill Pain Questionnaire was main efficacy variable; Global Evaluation score also measured at each follow-up visit
- Each participant received 4 intravenous blocks at 4 day intervals
- Randomization was into one of three groups
    - Group 1 (n=20) received 1 injection (the second) of guanethidine and 3 injections of saline placebo
    - Group 2 (n=19) received 2 injections of guanethidine (the second and third injections) and 2 of saline (the first and fourth)
    - Group 3 (n=18) received 4 injections of guanethidine
- After 1st injection, saline groups (#1 and #2) did not differ overall from guanethidine group (#3) in PRI score; the pain actually decreased slightly more in the placebo groups than in the guanethidine group, but not by a statistically significant amount
- Follow-up visits were scheduled after the 4th injection and again at 1 mo, 3 mo, and 6 mo
    - All three groups showed improvements in pain scores from baseline between the last injection and the last follow-up visit
    - The three groups did not differ from one another in the amount of improvement during follow-up
- At 6 mo follow-up, all groups had improved equally from baseline PRI scores and had equal improvements on Global Assessment
- No treatment group improved in range of motion from baseline, but all had equal improvements in edema, sudomotor, vasomotor, and trophic symptoms

Authors' conclusions:

- Placebo is as effective as guanethidine in improving pain scores in RSD, perhaps because of tourniquet, interactions with physicians, and repeated measurements, or co-administration of lidocaine to all groups

Comments:

- Power to detect between-group difference not stated; since groups are fairly small, study may have been underpowered to detect difference
- The inclusion criteria for CRPS (allodynia, hyperalgesia, and/or hyperesthesia) do not include any objective criteria; skin temperatures were measured but abnormalities of skin temperature were not used to define entry criteria for CRPS; similarly, vasomotor and sudomotor measurements were taken but were not part of the CRPS definition
- Therefore, the study population may have included people who did not have CRPS
- Because the study may have been underpowered and may have included patients with conditions other than CRPS, it is inconclusive regarding the effectiveness of guanethidine

Assessment: Inadequate for evidence about the effectiveness or ineffectiveness of guanethidine for CRPS